Docket No.: 19226/835 (R-5285, R-5321, R-5323, and R-5356

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants Prasad et al. Serial No. 09/265,625

Filed March 10, 1999

For TWO-PHOTON UPCONVERTING DYES

AND APPLICATIONS

3-11-03 3-11-03 Art Unit: 1614

)

Examiner: To Be Assigned

REQUEST FOR DECLARATION OF INTERFERENCE

Honorable Commissioner for Patents and Trademarks Washington, D.C. 20231

Sir:

Pursuant to 37 C.F.R. § 1.607(a), applicants hereby requests that an interference be declared between the above-identified application and U.S. Patent No. 5,829,448 to Fisher, et al. ("'448 patent"). Both the '448 patent and the claims of the present application relate to a method of treating a particular volume of living tissue with at least one photo-active molecular agent and with light to promote a simultaneous (or pumped) twophoton excitation of at least one of the at least one photo-active molecular agent. This treatment causes the at least one excited photo-active molecular agent to become photoactivated in the particular volume of the living tissue. As demonstrated infra, the earlier of applicants' filing date or effective filing date is prior to that of the '448 patent. An interference should, therefore, be instituted between applicant's above-identified application and the '448 patent.

I. INFORMATION IN SUPPORT OF DECLARING AN INTERFERENCE.

37 C.F.R. § 1.607(a) provides:

- An applicant may seek to have an interference declared between an application and an unexpired patent by,
 - (1) Identifying the patent,
 - (2) Presenting a proposed count,

- (3) Identifying at least one claim in the patent corresponding to the proposed count,
- (4) Presenting at least one claim corresponding to the proposed count or identifying at least one claim already pending in its application that corresponds to the proposed count, and, if any claim of the patent or application identified as corresponding to the proposed count does not correspond exactly to the proposed count, explaining why each such claim corresponds to the proposed count, and
- (5) Applying the terms of any application claim,
 - (i) Identified as corresponding to the count, and
- (ii) Not previously in the application to the disclosure of the application.

A. <u>Identification of Patent</u>.

It is requested that the present application be put into interference with the '448 patent in which Walter G. Fisher, Eric A. Wachter, and H. Craig Dees are named inventors and Photogen, Inc. is the assignee. The application corresponding to the '448 patent (i.e., U.S. Patent Application Serial No. 739,801) was filed on October 30, 1996, and the '448 patent was issued on November 3, 1998. The claims of the '448 patent are only entitled to the October 30, 1996, filing date of U.S. Patent Application Serial No. 739,801.

The present application, filed on March 10, 1999, is a division of U.S. Patent Application Serial No. 08/712,143 ("parent application"), filed September 5, 1996, now U.S. Patent No. 5,912,257, which claims the benefit of U.S. Provisional Patent Application Serial No. 60/003,296, filed September 6, 1995; U.S. Provisional Patent Application Serial No. 60/005,924, filed October 27, 1995; U.S. Provisional Patent Application Serial No. 60/010,330 ("grandparent application"), filed December 15, 1995; and U.S. Provisional Patent Application Serial No. 60/025,798, filed August 27, 1996. The present divisional application uses the same disclosure as the parent application and includes the disclosure of the grandparent application, both of which support all pending claims, pursuant to 35 U.S.C. § 112 (first paragraph), as demonstrated infra. Upon grant of the accompanying petition under 37 C.F.R. § 1.48(b) ("petition"), both the present application and the grandparent application identify Paras N. Prasad, Jayant D. Bhawalkar, Guange S. He, Chan F. Zhao, and Jaroslaw Zieba as inventors. The parent application additionally lists Raz Gvishi, Gary E.

Ruland, Ping Chin Cheng, and Shan Jen Pan as co-inventors. However, as noted in the petition, Raz Gvishi, Gary E. Ruland, Ping Chin Cheng, and Shan Jen Pan only contributed to the invention of claims 1-169 and 199-289 of the parent application which have been cancelled from this case. The Research Foundation of State University of New York is the assignee of the present application, the parent application, and all the aforementioned provisional applications. As shown <u>infra</u>, the claims of the present application are entitled to the December 15, 1995, filing date of the grandparent application.

B. Proposed Count.

Applicants propose the following count for purposes of initiating this interference:

Claim 290 of U.S. Patent Application Serial No. 09/265,625 ("'625

application")

or

Claim 299 of the '625 application

or

Claim 311 of the '625 application

or

Claim 313 of the '625 application

or

Claim 321 of the '625 application

or

Claim 1 of the '448 patent

or

Claim 10 of the '448 patent

or

Claim 24 of the '448 patent

or

Claim 27 of the '448 patent

or

Claim 29 of the '448 patent

or

Claim 40 of the '448 patent

or

Claim 52 of the '448 patent

or

Claim 62 of the '448 patent

C. Claims of U.S. Patent No. 5, 829, 448 Corresponding to the Proposed Count.

It is submitted that claims 1-68 of the '448 application correspond to the proposed count.

D. <u>Claims of the Present Application Corresponding to the Proposed</u>
Count.

Claims 290-325 of the present application correspond to the proposed count.

E. <u>Identification of Descriptive Support for the Claims Corresponding to the Proposed Count in the Original Disclosure of the Present Application.</u>

New claims 290-325 of the present application, which correspond to the proposed count, are descriptively supported by the original disclosure of the present application as follows:

Claims of the Present Application

290. A method for the treatment of a particular volume of living tissue, the method comprising the steps of:

a) treating the living tissue with at least one photo-active molecular agent, wherein the particular volume of the living tissue retains at

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

Specification, page 65, line 17; page 65, lines 25-30; page 70, lines 18-24; page 72, lines 11-13; page 72, lines 16-17; page 73, lines 7-9.

Specification, page 65, lines 18-19; page 65, lines 31-39; page 67, lines 20-24; page 68, lines 11-14; page 70, lines 30-32.

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

least a portion of the at least one photo-active molecular agent; and

b) treating the particular volume of the living tissue with light to promote a simultaneous two-photon excitation of at least one of the at least one photo-active molecular agent retained in the particular volume of the living tissue, wherein the at least one excited photo-active molecular agent becomes photo-activated in the particular volume of the living tissue.

Specification, page 1, lines 36-page 2, line 1; page 15, lines 2-5; page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 69, lines 32-37; page 70, lines 21-22.

291. The method of claim 290, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a laser light.

Specification, page 68, lines 27-28.

292. The method of claim 291, wherein the laser light is a pulsed laser light.

Specification, page 69, lines 5-14.

293. The method of claim 290, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a focused beam of light.

Specification, page 69, lines 20-25.

294. The method of claim 293, wherein the focused beam of light is focused laser light.

Specification, page 69, lines 20-25.

295. The method of claim 294, wherein the focused laser light is pulsed laser light.

Specification, page 69, lines 5-18.

296. The method of claim 290, wherein the at least one photo-active molecular agent is selected from the group consisting of haematoporphyrin

Specification, page 66, lines 1-39; page 67, lines 1-38.

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derivatives, dihematoporphyrin ether, porphyrins and porphyrin analogs, phthalocyanines and phthalocyanine analogs, rhodamine and rhodamine analogs, rhodamine B, rhodamine dyes, coumarin dyes, chlorophyll derivatives derived from bacteria and plants, stilbene dyes, hydrobenzoporphyrins, texaphyrin, furocourmarin, methoxsalen, bergapten, purpins, verdins, dimethyl POPOP, 1,3,1'3'-tetramethyl-2,2'-deoxopyrimide-6,6'-carbocyanine hydrogen sulfate, 4-dicyanomethylene-2-methyl-6-p-dimethylaminostyryl-4H-pyran, and analogs thereof, and styryl dyes.

297. The method of claim 290, wherein the at least one photo-active molecular agent includes at least one photo-active molecular agent that is specific to a particular tissue within the particular volume of living tissue being treated.

Specification, page 67, lines 20-24; page 72, lines 16-20.

298. The method of claim 297, wherein the at least one photo-active molecular agent includes a segment selected from the group consisting of antibodies, ligands, lipids, and encapsulating vehicles.

Specification, page 72, line 21-page 75, line 21.

299. A method for the treatment of cancer in living tissue, the method comprising the steps of:

Specification, page 65, line 17; page 65, lines 25-30; page 70, lines 18-24; page 72, lines 11-13; page 72, lines 16-17; page 73, lines 6-9.

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- (a) treating the living tissue with at least one photo-active molecular agent, wherein the cancer in the living tissue retains at least a portion of the at least one photo-active molecular agent; and
- Specification, page 65, lines 18-19; page 65, lines 31-39; page 67, lines 20-24; page 68, lines 11-12; page 70, lines 30-32.
- (b) treating the living tissue with light to promote a simultaneous two-photon excitation of at least one of the at least one photo-active molecular agent retained in the cancer in the living tissue, wherein the at least one photo-active molecular agent becomes photo-activated in the cancer in the living tissue.

Specification, page 1, line 36-page 2, line 1; page 15, lines 2-5; page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 69, lines 32-37; page 70, lines 21-22.

300. The method of claim 299, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a laser light.

Specification, page 68, lines 27-28.

301. The method of claim 300, wherein the laser light is a pulsed laser light.

Specification, page 69, lines 5-14.

302. The method of claim 299, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a focused beam of light.

Specification, page 69, lines 20-25.

303. The method of claim 302, wherein the focused beam of light is a focused laser light.

Specification, page 69, lines 20-25.

304. The method of claim 303, wherein the focused laser light is a pulsed laser light.

Specification, page 69, lines 5-14.

√3.0*5*\. The method of claim 299, wherein the at least one photo-active molecular agent is selected from the group consisting of haematoporphyrin derivatives, dihematoporphyrin ether, porphyrins and porphyrin analogs, phthalocyanines and phthalocyanine analogs, rhodamine and rhodamine analogs, rhodamine B, rhodamine dyes, coumarin dyes, chlorophyll derivatives derived from bacteria and plants, stilbene dyes, hydrobenzoporphyrins, texaphyrin, furocourmarin, methoxsalen, bergapten, purpins, verdins, dimethyl POPOP, 1,3,1'3'-tetramethyl-2,2'-deoxopyrimide-6,6'-carbocyanine hydrogen sulfate, 4-dicyanomethylene-2-methyl-6-pdimethylaminostyryl-4H-pyran and analogs thereof, and styryl dyes.

306. The method of claim 299, wherein the at least one photo-active molecular agent includes at least one photo-active molecular agent that is specific to a particular tissue within the particular volume of living tissue being treated.

307. The method of claim 306, wherein the at least one photo-active molecular agent includes a segment selected from the group consisting of antibodies, ligands, lipids, and encapsulating vehicles.

<u>Descriptive Support in U.S. Patent</u> Application Serial No. 09/265,625

Specification, page 66, lines 1-9; page 67, lines 1-38.

Specification, page 67, lines 20-24; page 72, lines 16-20.

Specification, page 72, line 21- page 75, line 21.

308. The method of claim 290, wherein said treating the particular volume of the living tissue includes focusing a beam of light so that a focal point of the light beam occurs at a position located between a surface of the tissue and a point substantially beyond the tissue surface, whereby said treating the particular volume of the living tissue may extend to penetrate deep within the tissue.

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

Specification, page 69, lines 20-31; page 70, lines 18-24.

309. The method of claim 308, wherein said treating the living tissue with light includes operating a laser to produce a pulsed output having a sub-nanosecond pulse duration.

Specification, page 68, lines 30-33; page 69, lines 5-8.

310. The method of claim 308, wherein the laser produces near-infrared light.

Specification, page 68, lines 30-33.

311. A method for medical treatment of a particular volume of tissue comprising the steps of:

Specification, page 65, line 17; page 65, lines 25-30; page 67, lines 20-24; page 70, lines 18-24; page 72, lines 11-13; page 72, lines 16-17; page 73, lines 7-9.

introducing a photo-active molecular agent into a tissue, said agent being selected to be absorbed and accumulated in the tissue, said agent being susceptible of two-photon excitation (TPE);

Specification, page 1, lines 36-page 2, line 1; page 15, lines 2-5; page 65, lines 18-19; page 65, lines 31-39; page 67, lines 27-28; page 68, lines 11-14; page 69, lines 16-18; page 70, lines 30-32.

allowing said agent to accumulate in specific tissue;

Specification, page 68, lines 15-18.

directing light to specific regions of interest within the tissue, including regions substantially Specification, page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 69,

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

below a tissue surface, said light being selected in frequency and energy to penetrate the tissue and to promote TPE substantially only at a focused region; lines 32-37; page 70, lines 21-22.

controlling the location of a focused region over a range of depths within said tissue; and

Specification, page 69, lines 16-25; page 70, lines 16-24.

using TPE to photoactivate said agent over said range of depth within the tissue, thereby producing photoactivated agents at the focused region.

Specification, page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 70, lines 16-24.

312. The method of claim 311, wherein said directing light includes generating near infra-red light with a pulsed laser operating at short pulse widths and a high pulse repetition rate, and focusing said laser into said tissue.

Specification, page 68, line 30-33; page 69, lines 5-20.

313. A method for the treatment of a particular volume of cancerous living tissue, the tissue including at least one photo-active molecular agent, the method comprising:

Specification, page 65, lines 17,-19; page 65, lines 22-30; page 67, lines 20-24; page 68, lines 15-18; page 68, lines 31-39; page 70, lines 18-24; page 72, lines 11-13; page 72, lines 16-17; page 73, lines 6-9.

treating said particular volume with light to promote simultaneous two-photon excitation of at least one of said at least one molecular agent so that said at least one excited molecular agent becomes photoactivated in said particular volume at a controllable position.

Specification, page 1, line 36-page 2, line 1; page 15, lines 2-5; page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 70, lines 21-22.

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

314. The method of claim 313, wherein said at least one excited molecular agent becomes photoactivated in said particular volume at a controllable position substantially beyond a tissue surface.

Specification, page 69, lines 20-25; page 70, lines 16-24.

315. The method of claim 313, further including varying a focal length position of said light within said tissue, thereby to photoactivate said at least one molecular agent along controlled positions between said tissue surface and a position located substantially beyond said tissue surface.

Specification, page 69, lines 20-25; page 70, lines 16-24.

316. The method of claim 313, wherein said treating includes directing a laser light to said particular volume.

Specification, page 68, lines 27-28.

317. The method of claim 316, wherein said treating includes directing a pulsed laser light to said particular volume.

Specification, page 69, lines 5-8.

318. The method of claim 317, wherein said laser is pulsed to produce sub-nanosecond duration pulses.

Specification, page 69, lines 5-7.

319. The method of claim 313 including operating a light source to produce near-infrared light.

Specification, page 68, line 27-page 69, line 4.

<u>Descriptive Support in U.S. Patent</u> <u>Application Serial No. 09/265,625</u>

320. The method of claim 317 including operating a light source to produce near-infrared light.

Specification, page 68, line 27-page 69, line 4.

321. A method for the medical treatment of a particular volume of tissue, wherein the tissue includes at least one photo-active molecular agent, the method comprising the steps of:

Specification, page 65, line 17; page 65, lines 24-30; page 67, lines 20-24; page 68, lines 15-18; page 68, lines 31-39; page 70, lines 18-20; page 72, lines 11-13; page 72, lines 16-17; page 73, lines 7-9.

directing light to specific regions of interest within the tissue, including regions substantially below a tissue surface, said light being selected to penetrate the tissue and to promote two photon excitation (TPE) substantially only at a focused region;

Specification, page 1, line 36-page 2, line 1; page 15, lines 2-5; page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25; page 70, lines 20-22.

controlling the location of said focused region over a range of depths within said tissue; and Specification, page 69, lines 20-25; page 70, lines 16-24.

using TPE, photoactivating at least one of said at least one molecular agent over said range of depths within said tissue, thereby producing at least one photo-activated agent substantially only at the focused region.

Specification, page 68, line 27-page 69, line 4; page 69, lines 15-25.

322. The method of claim 321, wherein said directing includes directing a laser light to said particular volume.

Specification, page 68, lines 27-28.

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- 323. The method of claim 322, wherein said directing includes directing a pulsed laser light to said particular volume.
- Specification, page 69, lines 5-8.
- 324. The method of claim 323, wherein said laser is operated to produce sub-nanosecond duration pulses.

Specification, page 69, lines 5-7.

325. The method of claim 321, wherein said method causes simultaneous TPE at said focused region.

Specification, page 1, lines 36-page 2, line 1; page 15, lines 2-5; page 67, lines 27-28; page 68, lines 19-20; page 68, line 27-page 69, line 4; page 69, lines 15-25.

II. THE CLAIMS OF U.S. PATENT NO. 5,829,448 ARE AT MOST ONLY ENTITLED TO A FILING DATE OF OCTOBER 30, 1996.

As discussed <u>supra</u>, U.S. Patent Application Serial No. 739,801, which issued as the '448 patent, was filed on October 30, 1996. The application does not claim priority from any previously filed application under 35 U.S.C. §§ 119, 120, or 365. Accordingly, the claims of the '448 patent are at most only entitled to a filing date of October 30, 1996.

III. THE CLAIMS OF THE PRESENT APPLICATION ARE ENTITLED TO A FILING DATE OF DECEMBER 15, 1995.

The present application was filed, pursuant to 37 C.F.R. § 1.53(b), as a division of U.S. Patent Application Serial No. 08/712,143 which was filed on September 5, 1996, now U.S. Patent No. 5,912,257. U.S. Patent Application Serial No. 08/712,142 claimed priority, under 35 U.S.C. § 119, to U.S. Provisional Patent Application Serial No. 60/010,330 filed December 15, 1995. A sentence stating this has been inserted at the beginning of the present application.

New claims 290-325 of the present application, which correspond to the proposed count, are descriptively supported by the original disclosure of the grandparent application as follows:

290. A method for the treatment of a particular volume of living tissue, the method comprising the steps of:

- a) treating the living tissue with at least one photo-active molecular agent, wherein the particular volume of the living tissue retains at least a portion of the at least one photo-active molecular agent; and
- b) treating the particular volume of the living tissue with light to promote a simultaneous two-photon excitation of at least one of the at least one photo-active molecular agent retained in the particular volume of the living tissue, wherein the at least one excited photo-active molecular agent becomes photo-activated in the particular volume of the living tissue.
- 291. The method of claim 290, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a laser light.
- 292. The method of claim 291, wherein the laser light is a pulsed laser light.

<u>Descriptive Support in U.S. Provisional</u> <u>Patent Application Serial No. 60/010,330</u>

Specification, page 5, line 16; page 5, lines 24-29; page 17, lines 20-26; page 19, lines 13-15; page 19, lines 18-19; page 20, lines 9-11.

Specification, page 5, lines 16-18; page 5, lines 30-38; page 7, lines 20-24; page 15, lines 12-15; page 17, lines 32-34.

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27; page 16, lines 34-39; page 17, lines 23-24; page 28, lines 10-29.

Specification, page 15, lines 28-29.

Specification, page 16, lines 7-16.

<u>Descriptive Support in U.S. Provisional</u> <u>Patent Application Serial No. 60/010,330</u>

293. The method of claim 290, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a focused beam of light.

Specification, page 16, lines 22-27.

294. The method of claim 293, wherein the focused beam of light is focused laser light.

Specification, page 16, lines 22-27.

295. The method of claim 294, wherein the focused laser light is pulsed laser light.

Specification, page 16, lines 7-20.

296. The method of claim 290, wherein the at least one photo-active molecular agent is selected from the group consisting of haematoporphyrin derivatives, dihematoporphyrin ether, porphyrins and porphyrin analogs, phthalocyanines and phthalocyanine analogs, rhodamine and rhodamine analogs, rhodamine B, rhodamine dyes, coumarin dyes, chlorophyll derivatives derived from bacteria and plants, stilbene dyes, hydrobenzoporphyrins, texaphyrin, furocourmarin, methoxsalen, bergapten, purpins, verdins, dimethyl POPOP, 1,3,1'3'-tetramethyl-2,2'-deoxopyrimide-6,6'-carbocyanine hydrogen sulfate, 4-dicyanomethylene-2-methyl-6-p-dimethylaminostyryl-4H-pyran, and analogs

Specification, page 6, lines 1-39; page 7, lines 1-page 15, line 1.

thereof, and styryl dyes.

Descriptive Support in U.S. Provisional Patent Application Serial No. 60/010,330

297. The method of claim 290, wherein the at least one photo-active molecular agent includes at least one photo-active molecular agent that is specific to a particular tissue within the particular volume of living tissue being treated.

Specification, page 7, lines 20-24; page 19, lines 18-22.

298. The method of claim 297, wherein the at least one photo-active molecular agent includes a segment selected from the group consisting of antibodies, ligands, lipids, and encapsulating vehicles.

Specification, page 19, line 23-page 22, line 23.

299. A method for the treatment of cancer in living tissue, the method comprising the steps of:

Specification, page 5, line 16; page 5, lines 24-29; page 17, lines 20-26; page 19, lines 13-15; page 19, lines 18-19; page 20, lines 9-11.

(a) treating the living tissue with at least one photo-active molecular agent, wherein the cancer in the living tissue retains at least a portion of the at least one photo-active molecular agent; and

Specification, page 5, lines 16-18; page 5, lines 30-38; page 7, lines 20-24; page 15, lines 12-15; page 17, lines 32-34.

(b) treating the living tissue with light to promote a simultaneous two-photon excitation of at least one of the at least one photo-active molecular agent retained in the cancer in the living tissue, wherein the at least one photo-active molecular agent becomes photo-activated in the cancer in the living tissue.

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27; page 16, lines 34-39; page 17, lines 23-24; page 28, lines 10-29.

300. The method of claim 299, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a laser light.

Specification, page 15, lines 28-29.

<u>Descriptive Support in U.S. Provisional</u> <u>Patent Application Serial No. 60/010,330</u>

301. The method of claim 300, wherein the laser light is a pulsed laser light.

Specification, page 16, lines 7-16.

302. The method of claim 299, wherein the light to promote a simultaneous two-photon excitation of the at least one photo-active molecular agent is a focused beam of light.

Specification, page 16, lines 22-27.

303. The method of claim 302, wherein the focused beam of light is a focused laser light.

Specification, page 16, lines 22-27.

304. The method of claim 303, wherein the focused laser light is a pulsed laser light.

Specification, page 16, lines 7-20.

305. The method of claim 299, wherein the at least one photo-active molecular agent is selected from the group consisting of haematoporphyrin derivatives, dihematoporphyrin ether, porphyrins and porphyrin analogs, phthalocyanines and phthalocyanine analogs, rhodamine and rhodamine analogs, rhodamine B, rhodamine dyes, coumarin dyes, chlorophyll derivatives derived from bacteria and plants, stilbene dyes, hydrobenzoporphyrins, texaphyrin, furocourmarin, methoxsalen, bergapten, purpins, verdins, dimethyl POPOP, 1,3,1'3'-tetramethyl-2,2'-deoxopyrimide-6,6'-carbocyanine hydrogen sulfate, 4-dicyanomethylene-2-methyl-6-p-

Specification, page 6, lines 1-9; page 7, lines 1-page 15, line 1.

306. The method of claim 299, wherein the at least one photo-active molecular agent includes at

dimethylaminostyryl-4H-pyran and analogs

thereof, and styryl dyes.

Specification, page 7, lines 20-24; page 19, lines 18-22.

Descriptive Support in U.S. Provisional Patent Application Serial No. 60/010,330

least one photo-active molecular agent that is specific to a particular tissue within the particular volume of living tissue being treated.

307. The method of claim 306, wherein the at least one photo-active molecular agent includes a segment selected from the group consisting of antibodies, ligands, lipids, and encapsulating vehicles.

Specification, page 19, line 23- page 22, line 23.

308. The method of claim 290, wherein said treating the particular volume of the living tissue includes focusing a beam of light so that a focal point of the light beam occurs at a position located between a surface of the tissue and a point substantially beyond the tissue surface, whereby said treating the particular volume of the living tissue may extend to penetrate deep within the tissue.

Specification, page 16, lines 22-33; page 17, lines 20-26.

309. The method of claim 308, wherein said treating the living tissue with light includes operating a laser to produce a pulsed output having a sub-nanosecond pulse duration.

Specification, page 15, lines 32-35; page 16, lines 7-10.

310. The method of claim 308, wherein the laser produces near-infrared light.

Specification, page 15, lines 32-35.

311. A method for medical treatment of a particular volume of tissue comprising the steps of:

Specification, page 5, line 16; page 5, lines 24-29; page 7, lines 20-23; page 17, lines 20-26; page 19, lines 13-15; page 19, lines 18-19; page 20, lines 9-11.

introducing a photo-active molecular agent into a tissue, said agent being selected to be absorbed and accumulated in the tissue, said agent being susceptible of two-photon excitation (TPE);

allowing said agent to accumulate in specific tissue;

directing light to specific regions of interest within the tissue, including regions substantially below a tissue surface, said light being selected in frequency and energy to penetrate the tissue and to promote TPE substantially only at a focused region;

controlling the location of a focused region over a range of depths within said tissue; and

using TPE to photoactivate said agent over said range of depth within the tissue, thereby producing photoactivated agents at the focused region.

312. The method of claim 311, wherein said directing light includes generating near infra-red light with a pulsed laser operating at short pulse widths and a high pulse repetition rate, and focusing said laser into said tissue.

<u>Descriptive Support in U.S. Provisional</u> <u>Patent Application Serial No. 60/010,330</u>

Specification, page 5, lines 16-18; page 5, lines 30-38; page 7, lines 27-28; page 15, lines 12-15; page 16, lines 18-20; page 17, lines 32-34.

Specification, page 15, lines 16-19.

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27; page 16, lines 34-39; page 17, lines 23-24.

Specification, page 16, lines 18-27; page 17, lines 18-26.

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27; page 17, lines 18-26.

Specification, page 15, line 31-35; page 16, lines 7-22.

313. A method for the treatment of a particular volume of cancerous living tissue, the tissue including at least one photo-active molecular agent, the method comprising:

treating said particular volume with light to promote simultaneous two-photon excitation of at least one of said at least one molecular agent so that said at least one excited molecular agent becomes photoactivated in said particular volume at a controllable position.

- 314. The method of claim 313, wherein said at least one excited molecular agent becomes photoactivated in said particular volume at a controllable position substantially beyond a tissue surface.
- 315. The method of claim 313, further including varying a focal length position of said light within said tissue, thereby to photoactivate said at least one molecular agent along controlled positions between said tissue surface and a position located substantially beyond said tissue surface.
- 316. The method of claim 313, wherein said treating includes directing a laser light to said particular volume.
- 317. The method of claim 316, wherein said treating includes directing a pulsed laser light to said particular volume.

<u>Descriptive Support in U.S. Provisional</u> <u>Patent Application Serial No. 60/010,330</u>

Specification, page 5, lines 16-18; page 5, lines 21-29; page 7, lines 20-23; page 15, lines 16-19; page 15, line 32-page 16, line 2; page 17, lines 20-26; page 19, lines 13-15; page 19, lines 18-20; page 20, lines 9-11.

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27; page 17, lines 23-24; page 28, lines 10-29.

Specification, page 16, lines 22-27; page 17, lines 17-26.

Specification, page 16, lines 22-27; page 17, lines 18-26.

Specification, page 15, lines 28-29.

Specification, page 16, lines 7-16.

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318. The method of claim 317, wherein said laser is pulsed to produce sub-nanosecond duration pulses.

Specification, page 16, lines 7-9.

319. The method of claim 313 including operating a light source to produce near-infrared light.

Specification, page 15, line 28-page 16, line 6.

320. The method of claim 317 including operating a light source to produce near-infrared light.

Specification, page 15, line 28-page 16, line 6.

321. A method for the medical treatment of a particular volume of tissue, wherein the tissue includes at least one photo-active molecular agent, the method comprising the steps of:

Specification, page 5, line 16; page 5, lines 23-29; page 7, lines 20-23; page 15, line 32-page 16, line 2; page 15, lines 16-19; page 17, lines 20-22; page 19, lines 13-17; page 19, lines 18-20; page 20, lines 9-11.

directing light to specific regions of interest within the tissue, including regions substantially below a tissue surface, said light being selected to penetrate the tissue and to promote two photon excitation (TPE) substantially only at a focused region;

Specification, page 15, lines 20-21; page 15, line 28-page 16, line 6; page 16, lines 17-27.

controlling the location of said focused region over a range of depths within said tissue; and Specification, page 16, lines 22-27; page 17, lines 18-26.

using TPE, photoactivating at least one of said at least one molecular agent over said range of depths within said tissue, thereby producing at least one photo-activated agent substantially only at the focused region.

Specification, page 15, line 28-page 16, line 6; page 16, lines 17-27.

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322. The method of claim 321, wherein said directing includes directing a laser light to said particular volume.

Specification, page 15, lines 28-29.

323. The method of claim 322, wherein said directing includes directing a pulses laser light to said particular volume.

Specification, page 16, lines 7-16.

324. The method of claim 323, wherein said laser is operated to produce sub-nanosecond duration pulses.

Specification, page 16, lines 7-10.

325. The method of claim 321, wherein said method causes simultaneous TPE at said focused region.

Specification, page 7, lines 27-28; page 15, lines 20-21; page 15, line 28-page 19, line 6; page 16, lines 17-27.

Thus, the claims of the present application are entitled to the December 15, 1995, filing date of the grandparent application.

IV. PRIMA FACIE SHOWING OF PRIORITY FOR THE PRESENT APPLICATION.

Under 37 C.F.R. § 1.608, a patent application is required to allege a basis upon which he is entitled to judgment before an interference will be declared between his application and a patent. When the earlier of the application's actual or effective filing date is three months or less <u>after</u> the earlier of the actual or effective filing date of the patent, the requirements of 37 C.F.R. § 1.608(a) govern. For greater time gaps, the provisions of 37 C.F.R. § 1.608(b) control. However, 37 C.F.R. § 1.608 is inapplicable where the effective filing date for the application is <u>before</u> that of the patent. In such cases, the applicant is not required to make a showing, because, pursuant to 37 C.F.R. § 1.657, there is a rebuttable presumption that inventors make "their invention in the chronological order of the earlier of their filing dates or effective filing dates." As a result, an applicant's earlier filing date is itself a facially sufficient basis upon which he is entitled to judgment.

Here, as demonstrated <u>supra</u>, the earlier of applicants' filing date or effective filing date (i.e. December 15, 1995) is before that of the '448 patent (i.e. October 30, 1996). This alone provides a <u>prima facie</u> basis for entitlement to judgment by applicants, Paras N. Prasad, Jayant D. Bhawalkar, Guange S. He, Chan F. Zhao, and Jaroslaw Zieba.

V. CONCLUSION.

Having met all the requirements of the Code of Federal Regulations, Title 37, applicants hereby submit that an interference between the present application and the '448 patent should be declared.

Respectfully submitted,

Date: October 25, 1989

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Jo Ann Whalen